Asian Journal of Chemistry; Vol. 36, No. 1 (2024), 177-183

ASIAN JOURNAL OF CHEMISTRY

https://doi.org/10.14233/ajchem.2024.30712

Effect of Substituent on the ^{13}C NMR Chemical Shifts of Substituted 26-Membered [2+2] Macrocyclic Compounds

PARATHARAJ SENTHILKUMAR[1] and KRISHNAN RADHAKRISHNAN[2,*]

[1]CRD Department, RECEPS Limited, Visakha Pharmacity Limited, Visakhapatnam-531019, India
[2]Department of Chemistry, Saraswathi Narayanan College of Arts and Science (Affiliated to Madurai Kamaraj University), Perungudi, Madurai-625022, India

*Corresponding author: E-mail: prskradha61@gmail.com; senthilkumarparatharaj@gmail.com

Received: 16 October 2023; *Accepted*: 28 November 2023; *Published online*: 31 December 2023; AJC-21500

A series of substituted symmetrical $1^4,1^5,3^4,3^5,9^4,9^5,11^4,11^5$-octamethoxy-2,10-*bis*(4-methoxyphenyl)-4,8,12,16-tetraaza-1,3,9,11(1,2),6,14(1,4)-hexabenzenacyclohexadecaphane-4,7,12,15-tetraene compounds (macrocyclic compounds) was synthesized by condensation of various substituted benzaldehyde with 1,2-dimethoxy benzene followed by nitration, reduction and cyclization with terephthaldehyde. Isolated substituted compounds were characterized by UV, IR, NMR and mass spectrometric techniques. Investigation of substituents effect and mode of transmission of electronic effects have been carried out by ^{13}C NMR chemical shifts measurement and correlated it with LFER parameters in substituted macrocyclic compounds.

Keywords: Substituent effects, Lynch correlations, Multiple regression analysis.

INTRODUCTION

In organic chemistry, Hammett equation is one of the famous and most effective and intensively examined experiential relationship to the quantitative exploration of reactivity. The Hammett equation explains a linear relationship connecting log k or log K of substituted benzoic acids. These correlations demonstrated as rate-rate, equilibrium-equilibrium or rate-equilibrium relationships. These relationships are frequently mentioned as linear free-energy relationships (LFER). The LFER has often been used to cover the whole correlation study in organic chemistry [1-3]. Modern studies show that Hammett parameters can be correlated with the reaction rates, equilibrium constants, IR frequencies, UV absorption and NMR chemical shifts [4-7]. Correlation of chemical shift with substituent constant used to identify the type of effect of the substituent on the physical property of the compounds [8-10]. The single substituent parameter (SSP) method has been applied to correlate the chemical shift of *m*- and *p*-substituted compounds to unsubstituted compounds using the σ_m and σ_p value as represented in eqn. 1 and the values of ^{13}C were calculated for *m*- and *p*- substituted cinnamic acids [11-13]. The dual substituent parameter (DSP) method yields the effect of substituent effect in to inductive (σ_I) and resonance (σ_R) parameters as represented in eqn. 2.

$$\delta = \rho\sigma + \delta^o \qquad (1)$$

$$\delta = \rho_I\sigma_I + \rho_R\sigma_R + \delta^o \qquad (2)$$

The substituent constant (σ), which is independent of nature of the reaction and measures the polar effect of the substituent. The reaction constant (ρ), which is depends on the nature of reaction and measures the sensitivity of the reaction to the influence of the substituents. Electron withdrawing substituents have positive σ value and electron releasing substances have negative σ value. The σ-scale covers roughly the numerical range 0 ± 1.4. The dual substitutent parameter (DSP) eqn. 2 is the most generally useful treatment and well-suited for the analysis of spectroscopic data. The values ρ_I and ρ_R are position dependant and give a direct measure of the transmission of inductive and resonance effects. The significance of resonance and inductive effects are represented by the blending factor (λ). Several authors [14-17] projected an eqn. 3 for identifying the influence of +M substituents on reactions. The DSP analysis of sterically congested systems has been improved by triple substituent parameter (TSP) by using Charton's steric parameter (ν) using eqn. 4:

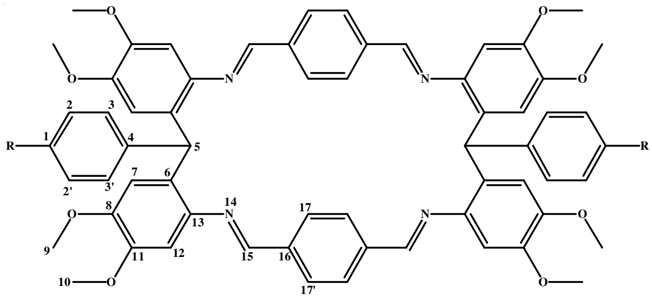
$$\delta = \rho\sigma + r(\sigma^{+} - \sigma^{-}) + \delta^{o} \qquad (3)$$

$$\delta = \rho_I\,\sigma_I + \rho_R\,\sigma_R + \varphi\nu + \delta^{o} \qquad (4)$$

Recently, we have reported the synthesis, characterization and antioxidant activity of novel 26 membered [2+2] macrocycles and the effect of substituents on the antimicrobial activities of substituted $1^4,1^5,3^4,3^5,9^4,9^5,11^4,11^5$-octamethoxy2,10-*bis*(4-methoxyphenyl) -4,8,12,16-tetraaza-1,3,9,11(1,2),6,14(1,4)-hexabenzenacyclohexadecaphane-4,7,12,15-tetraene derivatives [18,19]. These reports prompted us to undertake a detailed ^{13}C NMR spectral correlation study of various substituted macrocyclic compounds.

EXPERIMENTAL

In this study, the substituted macrocyclic compounds (Fig. 1) were synthesized in order to study the correlations using the Hammett substituent constants and ^{13}C NMR substituent induced chemical shifts (SCS) of substituted macrocyclic compounds. Additionally, SCS was also used to monitor the electronic effects in molecular structures and to understand long-range effects in extended π-systems.



R= $-OCH_3$, $-CH_3$, $-CH_2CH_3$, -H, -Cl, $-COOCH_3$, -COOH.

Fig. 1. Chemical structure of macrocyclic compounds

Assignment of ^{13}C chemical shifts: The ^{13}C chemical shifts were assigned by the intensity and substituent-induced chemical shifts (SCS) considerations. The ^{13}C chemical shifts of the substituted $1^4,1^5,3^4,3^5,9^4,9^5,11^4,11^5$-octamethoxy-2,10-*bis*(4-methoxyphenyl)-4,8,12,16-tetraaza-1,3,9,11(1,2),6,14 (1,4)-hexabenzen acyclohexadecaphane-4,7,12,15-tetraene compounds are presented in Table-1.

RESULTS AND DISCUSSION

Substituent effects on the ^{13}C NMR chemical shifts of substituted macrocyclic compounds: The ^{13}C chemical shift data of several carbon atoms of substituted compounds has been correlated with the SSP (eqn. 1), DSP (eqn. 2) and Yukawa-Tsuno (eqn. 3) correlations.

Correlations with Lynch equation: In case of C_1, there is a good correlation with (r = 0.998) appropriate SCS (S_I) values and slope b is 0.921, which discloses that the fixed substituent $Y = C_{25}H_{23}N_2O_4$, has little effect on the additivity of this shifts [20-25]. A good correlation exists between SCS of $C_{22'}$ and S_o with a correlation coefficient (r = 0.997) and the slope value (b = 0.966), indicating that the fixed substituent Y, has little effect on the additivity of these shifts [20-25]. A poor correlation exists between SCS of $C_{33'}$ and S_m with a correlation coefficient (r = 0.818) and the slope value (b = 0.599) discloses that the fixed substituent Y diminishes the substituent effect [26]. The C_4 carbon affords a good correlation with S_p with a correlation coefficient r = 0.946 and the slope value b = 0.901 demonstrates that the fixed substituent Y diminishes the substituent effect [26]. The outcomes of Lynch correlations are given in Table-2 and the plots of Lynch correlations are shown in Fig. 2 using Lynch eqn. 5:

$$SCS_X\,(Y) = a + b\,[SCS_X\,(H)] \qquad (5)$$

Hammett and dual substituent parameter correlations: Hammett equation is one of the famous most successful and intensively investigated empirical relationships to the quantitative exploration of reactivity in organic chemistry. The Hammett equation explains a linear relationship connecting log k or log K of substituted benzoic acids. Such correlations may be demonstrated as rate-rate, equilibrium-equilibrium or rate-equilibrium relationships and are usually referred to as linear free energy relationships (LFER). The ^{13}C chemical shifts of the carbon atoms of the macrocyclic compound series afford several reasonable correlations using Hammett substituent parameters eqn. 1 and the data are given in Table-3 [20-26].

The outcomes of the correlations of ^{13}C SCS values of macrocyclic compounds series with σ_I and σ_R constants according to eqn. 2 are presented in Table-4, whereas the outcomes

TABLE-1
^{13}C NMR CHEMICAL SHIFTS OF SUBSTITUTED MACROCYCLIC COMPOUNDS

Substituent (R)	1	2/2’	3/3’	4	5	6/6’	7/7’	8/8’
$-OCH_3$	157.57	113.37	130.01	137.40	42.25	130.56	113.47	147.93
$-CH_3$	135.09	128.98	128.98	142.16	42.65	130.47	113.43	147.93
$-CH_2CH_3$	142.36	127.57	129.01	141.42	42.67	130.51	113.50	147.94
-H	125.71	129.10	128.08	145.42	43.03	130.28	113.49	148.01
-Cl	131.47	128.87	129.83	143.97	42.45	130.42	113.21	148.19
$-COOCH_3$	127.71	129.44	129.07	147.70	43.16	129.59	113.26	148.26
-COOH	126.87	130.11	129.16	152.06	43.17	129.44	113.23	148.28
Substituent (R)	**9/9’**	**10/10’**	**11/11’**	**12/12’**	**13/13’**	**15/15’**	**16/16’**	**17/17’**
$-OCH_3$	56.19	56.01	147.39	101.65	142.81	157.11	138.63	128.84
$-CH_3$	56.20	56.01	147.37	101.64	142.88	157.12	138.63	128.83
$-CH_2CH_3$	56.22	56.01	147.38	101.66	142.92	157.16	138.63	128.84
-H	56.19	56.02	147.42	101.65	142.89	157.10	138.64	128.84
-Cl	56.23	56.03	147.56	101.64	142.80	157.09	138.65	128.87
$-COOCH_3$	56.20	56.03	147.59	101.64	142.80	157.07	138.65	128.87
-COOH	56.21	56.03	147.61	101.69	142.80	157.20	138.63	128.91

TABLE-2
RESULTS OF LYNCH CORRELATIONS (5) OF ^{13}C CHEMICAL SHIFTS OF
COMPOUND Fig. 1 WITH SCS VALUES FOR MONOSUBSTITUTED BENZENES

Carbons	Benzene SCS (S)[a]	Slope	Intercept	r[b]	n[c]	s[d]
C_1	S_I	0.921	-115.12	0.998	7	0.697
$C_{22'}$	S_o	0.966	-124.18	0.997	7	0.371
$C_{33'}$	S_m	0.599	-77.097	0.818	7	0.292
C_4	S_p	0.901	-130.99	0.946	7	1.589

where ‘a’ is SCS value, ‘b’ is the Correlation coefficient, ‘c’ is the Number of data points, ‘d’ is Standard deviations

TABLE-3
RESULTS OF STATISTICAL TREATMENT OF ^{13}C – CHEMICAL SHIFT WITH
σ_p, σ_p^o, σ_p^+, σ_p^-, σ_p^+/σ_p, σ_p/σ_p^-, σ_p^+/σ_p^- -SUBSTITUENT CONSTANTS USING SINGLE PARAMETER eqn. 1

Carbon	Scale	ρ	r	s	F	log(IZD)°	n
C_1	σ_p	-0.113 ± 0.020	0.956	0.014	31.644	2.152 ± 0.010	5
	σ_p^o	-0.082 ± 0.071	0.553	0.038	1.325	2.138 ± 0.020	5
	σ_p^+	-0.074 ± 0.010	0.987	0.010	117.261	2.135 ± 0.003	5
	σ_p^-	-0.071 ± 0.021	0.888	0.021	11.165	2.154 ± 0.011	5
	σ_p^+/σ_p	-0.074 ± 0.004	0.996	0.004	391.43	2.137 ± 0.002	5
	σ_p/σ_p^-	-0.073 ± 0.021	0.898	0.020	12.442	2.155 ± 0.011	5
	σ_p^+/σ_p^-	-0.057 ± 0.010	0.970	0.011	47.374	2.143 ± 0.010	5
C_4	σ_p	0.042 ± 0.010	0.801	0.010	20.099	2.156 ± 0.003	7
	σ_p^o	0.046 ± 0.021	0.78	0.012	4.655	2.154 ± 0.010	5
	σ_p^+	0.030 ± 0.010	0.935	0.010	34.571	2.161 ± 0.002	7
	σ_p^-	0.030 ± 0.010	0.897	0.010	20.479	2.155 ± 0.003	7
	σ_p^+/σ_p	0.030 ± 0.010	0.924	0.010	29.406	2.160 ± 0.002	7
	σ_p/σ_p^-	0.030 ± 0.010	0.900	0.010	21.304	2.154 ± 0.003	7
	σ_p^+/σ_p^-	0.023 ± 0.003	0.949	0.005	45.087	2.158 ± 0.002	7
C_6	σ_p	-0.005 ± 0.001	0.890	0.001	18.977	2.115 ± 0.000	7
	σ_p^o	-0.004 ± 0.002	0.735	0.001	3.515	2.115 ± 0.001	5
	σ_p^+	-0.003 ± 0.001	0.845	0.001	12.453	2.114 ± 0.000	7
	σ_p^-	-0.003 ± 0.000	0.963	0.000	63.18	2.115 ± 0.000	7
	σ_p^+/σ_p	-0.003 ± 0.001	0.808	0.001	9.414	2.114 ± 0.000	7
	σ_p/σ_p^-	-0.003 ± 0.000	0.962	0.000	62.689	2.115 ± 0.000	7
	σ_p^+/σ_p^-	-0.002 ± 0.001	0.907	0.001	23.059	2.115 ± 0.000	7
C_8	σ_p	0.002 ± 0.000	0.986	0.000	169.683	2.170 ± 0.000	7
	σ_p^o	0.002 ± 0.000	0.997	0.000	467.801	2.170 ± 0.000	5
	σ_p^+	0.001 ± 0.000	0.898	0.000	20.792	2.171 ± 0.000	7
	σ_p^-	0.001 ± 0.000	0.958	0.000	55.803	2.170 ± 0.000	7
	σ_p^+/σ_p	0.001 ± 0.000	0.912	0.000	24.78	2.171 ± 0.000	7
	σ_p/σ_p^-	0.001 ± 0.000	0.956	0.000	52.88	2.170 ± 0.000	7
	σ_p^+/σ_p^-	0.001 ± 0.000	0.934	0.000	34.14	2.170 ± 0.000	7
C_{15}	σ_p	-0.000 ± 0.000	0.961	0.000	36.469	2.196 ± 0.000	5
	σ_p^o	-0.000 ± 0.000	0.983	0.000	56.354	2.196 ± 0.000	4
	σ_p^+	-0.000 ± 0.000	0.837	0.000	7.027	2.196 ± 0.000	5
	σ_p^-	-0.000 ± 0.000	0.964	0.000	39.845	2.196 ± 0.000	5
	σ_p^+/σ_p	-0.000 ± 0.000	0.831	0.000	6.707	2.196 ± 0.000	5
	σ_p/σ_p^-	-0.000 ± 0.000	0.963	0.000	38.244	2.196 ± 0.000	5
	σ_p^+/σ_p^-	-0.000 ± 0.000	0.888	0.000	11.136	2.196 ± 0.000	5
C_5	σ_p	0.009 ± 0.004	0.711	0.003	5.119	1.630 ± 0.001	7
	σ_p^o	0.007 ± 0.008	0.438	0.004	0.714	1.630 ± 0.002	5
	σ_p^+	0.007 ± 0.002	0.825	0.002	10.626	1.632 ± 0.001	7
	σ_p^-	0.006 ± 0.002	0.760	0.003	6.847	1.630 ± 0.001	7
	σ_p^+/σ_p	0.006 ± 0.002	0.770	0.003	7.285	1.631 ± 0.001	7
	σ_p/σ_p^-	0.007 ± 0.002	0.767	0.003	7.162	1.633 ± 0.001	7
	σ_p^+/σ_p^-	0.005 ± 0.002	0.822	0.002	10.389	1.631 ± 0.001	7

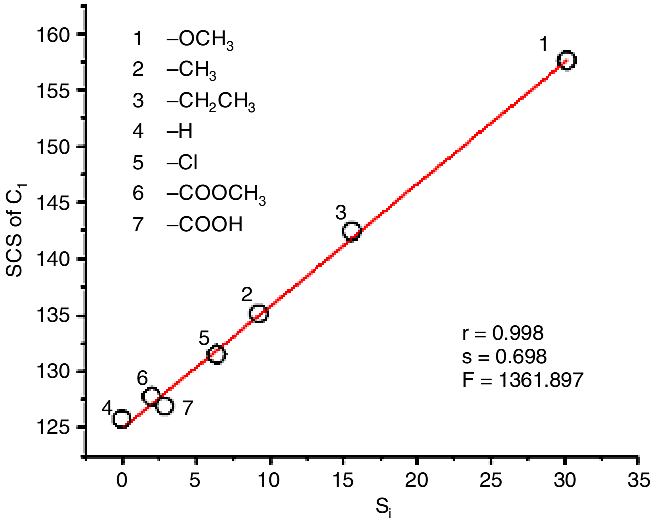


Fig. 2. Lynch plot of SCS of C_1 *vs.* Si

of multiple regression analysis of ^{13}C chemical shift with σ_p, $(\sigma_p^+ - \sigma_p)$ and σ_p^o, $(\sigma_p^+ - \sigma_p^o)$ constants using eqn. 3 are presented in Table-5.

C_1 – carbon atom: The chemical shift of C_1 carbon appeared over a range of 31.86 ppm. The outcome of the SSP analysis is shown in Table-3; a fairly good correlation afforded by σ_P^+/σ_P constant is given in eqn. 6. The plot of log δC_1 *vs.* σ_P^+/σ_P is shown in Fig. 3.

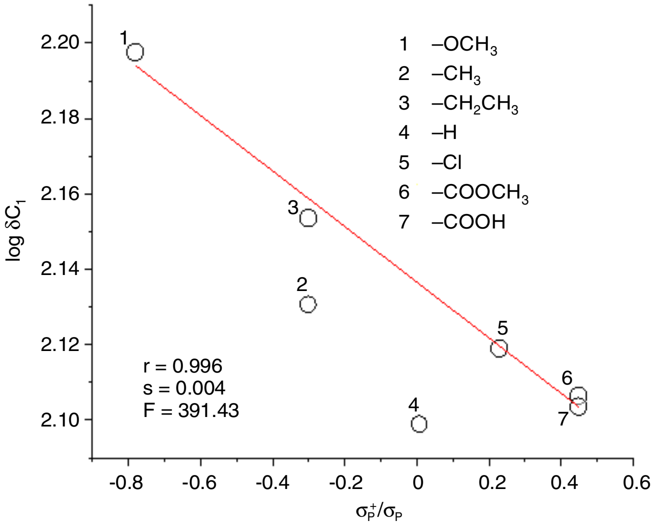


Fig. 3. Plot of log δC_1 *vs.* σ_P^+/σ_P

$$\log \delta C_1 = -0.074\ (\pm\ 0.004)\ \sigma_P^+/\sigma_P + 2.137\ (\pm\ 0.002) \qquad (6)$$

$$r = 0.996;\ s = 0.004;\ F = 391.43;\ n = 5$$

TABLE-4
DSP ANALYSIS OF CHEMICAL SHIFT DATA WITH DUAL PARAMETER eqn. 2

Carbon	Scale	ρ_I	ρ_R	R	SE	F	log (IZD)°	n	$\lambda = \rho_R/\rho_I$
C_1	σ_I, σ_R	-0.101 ± 0.020	-0.164 ± 0.020	0.996	0.01	67.668	2.125 ± 0.010	4	1.62
	σ_I, σ_R^o	-0.100 ± 0.100	-0.119 ± 0.041	0.915	0.023	5.149	2.149 ± 0.020	5	1.53
	σ_I, σ_R^+	-0.100 ± 0.032	-0.100 ± 0.011	0.977	0.012	20.610	2.136 ± 0.010	5	1.30
	σ_I, σ_R^-	-0.100 ± 0.093	-0.153 ± 0.100	0.881	0.034	1.731	2.132 ± 0.033	4	1.55
	F, R	-0.100 ± 0.040	-0.129 ± 0.023	0.974	0.013	18.444	2.138 ± 0.013	5	1.78
C_4	σ_I, σ_R	0.040 ± 0.020	0.064 ± 0.020	0.881	0.01	5.188	2.163 ± 0.010	6	1.58
	σ_I, σ_R^o	0.020 ± 0.010	0.100 ± 0.010	0.983	0.003	59.063	2.159 ± 0.002	7	3.19
	σ_I, σ_R^+	-0.002 ± 0.020	0.020 ± 0.010	0.838	0.01	4.701	2.166 ± 0.010	7	12.76
	σ_I, σ_R^-	0.043 ± 0.010	0.080 ± 0.010	0.990	0.003	77.778	2.164 ± 0.002	6	1.84
	F, R	0.022 ± 0.011	0.056 ± 0.010	0.960	0.005	23.336	2.162 ± 0.003	7	2.55
C_6	σ_I, σ_R	-0.004 ± 0.003	-0.004 ± 0.003	0.649	0.001	1.089	2.115 ± 0.001	6	1.14
	σ_I, σ_R^o	-0.003 ± 0.001	-0.006 ± 0.001	0.959	0.001	23.181	2.115 ± 0.000	7	2.10
	σ_I, σ_R^+	-0.001 ± 0.003	-0.002 ± 0.001	0.775	0.001	3.012	2.114 ± 0.001	7	1.85
	σ_I, σ_R^-	-0.004 ± 0.001	-0.010 ± 0.002	0.930	0.001	9.608	2.114 ± 0.000	6	1.55
	F, R	-0.004 ± 0.002	-0.005 ± 0.001	0.899	0.001	8.461	2.115 ± 0.001	7	1.38
C_8	σ_I, σ_R	0.002 ± 0.000	0.001 ± 0.000	0.950	0.000	14.022	2.170 ± 0.000	6	0.69
	σ_I, σ_R^o	0.002 ± 0.000	0.001 ± 0.000	0.993	0.000	148.010	2.170 ± 0.000	7	0.84
	σ_I, σ_R^+	0.001 ± 0.000	0.000 ± 0.000	0.926	0.000	12.057	2.170 ± 0.000	7	0.40
	σ_I, σ_R^-	0.002 ± 0.000	0.002 ± 0.000	0.981	0.000	37.418	2.170 ± 0.000	6	0.80
	F, R	0.002 ± 0.000	0.001 ± 0.000	0.999	0.000	712.431	2.170 ± 0.000	7	0.72
C_{15}	σ_I, σ_R	-0.000 ± 0.000	-0.000 ± 0.000	0.982	0.000	13.833	2.196 ± 0.000	4	0.52
	σ_I, σ_R^o	-0.000 ± 0.000	-0.000 ± 0.000	0.988	0.000	40.177	2.196 ± 0.000	5	0.94
	σ_I, σ_R^+	-0.000 ± 0.000	-0.000 ± 0.000	0.891	0.000	3.840	2.196 ± 0.000	5	0.52
	σ_I, σ_R^-	-0.000 ± 0.000	-0.000 ± 0.000	0.999	0.000	248.264	2.196 ± 0.000	4	0.72
	F, R	-0.000 ± 0.000	-0.000 ± 0.000	0.825	0.000	3.187	2.196 ± 0.000	6	0.47
C_5	σ_I, σ_R	0.002 ± 0.010	0.014 ± 0.010	0.821	0.003	3.100	1.633 ± 0.002	6	6.81
	σ_I, σ_R^o	-0.001 ± 0.002	0.016 ± 0.002	0.965	0.001	26.798	1.632 ± 0.001	7	10.58
	σ_I, σ_R^+	-0.007 ± 0.010	0.010 ± 0.002	0.853	0.002	5.332	1.634 ± 0.001	7	0.78
	σ_I, σ_R^-	0.003 ± 0.002	0.020 ± 0.002	0.985	0.001	47.353	1.633 ± 0.000	6	6.12
	F, R	-0.001 ± 0.003	0.015 ± 0.003	0.948	0.001	17.576	1.633 ± 0.001	7	17.81

TABLE-5
RESULTS OF MULTIPLE REGRESSION ANALYSIS OF ^{13}C CHEMICAL SHIFTS WITH σ_p, $(\sigma_p^+ - \sigma_p)$ AND σ_p^o, $(\sigma_p^+ - \sigma_p^o)$ CONSTANTS USING YUKAVA-TSUNO eqn. 3

Carbon	Scale	ρ	r	R	SE	F	n
C_1	$\sigma_p, (\sigma_p^+ - \sigma_p)$	-0.020 ± 0.023	-0.165 ± 0.040	0.960	0.012	23.793	7
	$\sigma_p^o, (\sigma_p^+ - \sigma_p^o)$	-0.021 ± 0.020	-0.137 ± 0.017	0.989	0.010	45.343	5
C_4	$\sigma_p, (\sigma_p^+ - \sigma_p)$	0.030 ± 0.012	0.030 ± 0.020	0.935	0.010	13.829	7
	$\sigma_p^o, (\sigma_p^+ - \sigma_p^o)$	0.030 ± 0.014	0.040 ± 0.014	0.954	0.010	10.197	5
C_6	$\sigma_p, (\sigma_p^+ - \sigma_p)$	-0.005 ± 0.002	0.000 ± 0.003	0.890	0.001	7.613	7
	$\sigma_p^o, (\sigma_p^+ - \sigma_p^o)$	-0.003 ± 0.003	-0.002 ± 0.003	0.785	0.001	1.605	5
C_8	$\sigma_p, (\sigma_p^+ - \sigma_p)$	0.002 ± 0.000	-0.001 ± 0.000	0.998	0.000	424.939	7
	$\sigma_p^o, (\sigma_p^+ - \sigma_p^o)$	0.002 ± 0.000	0.000 ± 0.000	0.997	0.000	184.519	5
C_{15}	$\sigma_p, (\sigma_p^+ - \sigma_p)$	-0.000 ± 0.000	0.000 ± 0.000	0.992	0.000	62.264	5
	$\sigma_p^o, (\sigma_p^+ - \sigma_p^o)$	-0.000 ± 0.000	0.000 ± 0.000	0.987	0.000	18.821	4

The chemical shift data in Table-1 shows that the electron releasing substituent causes a downfield shift whereas the electron withdrawing substituent causes an upfield shift. The DSP analysis of C_1 carbon with various σ_R scale is given in Table-4. The excellent correlation is given in eqns. 7 and 8.

$$\log \delta C_1 = -0.101 (\pm 0.020)\ \sigma_I - 0.164 (\pm 0.020)\ \sigma_R + 2.125 (\pm 0.010) \quad (7)$$

$R = 0.996;\ SE = 0.010;\ F = 67.668;\ n = 4$

$$\log \delta C_1 = -0.100 (\pm 0.040)\ F - 0.129 (\pm 0.023)\ R + 2.138 (\pm 0.013 \quad (8)$$

$R = 0.974;\ SE = 0.013;\ F = 18.444;\ n = 5$

The value of slopes ρ_I and ρ_R are negative, which discloses that the reverse substituent effect activates on C_1 carbon atom. The results of the Yukawa-Tsuno correlation (eqn. 3) is given in Table-5, while the highest fit is given in eqn. 9:

$$\log \delta C_1 = -0.021 (\pm 0.020)\ \sigma_p^o - 0.137 (\pm 0.017)\ (\sigma_p^+ - \sigma_p^o) + 2.103 (\pm 0.006) \quad (9)$$

$R = 0.989;\ SE = 0.01;\ F = 45.343;\ n = 5$

C_4–carbon atom: The chemical shift of C_4 carbon appeared over a range of 14.66 ppm. The results of the SSP analysis is shown in Table-3; a fairly good correlation afforded by σ_p^+/σ_p^- constant is given in eqn. 10.

$$\log \delta C_4 = 0.023 (\pm 0.003)\ \sigma_P^+/\sigma_P^- + 2.158 (\pm 0.002) \quad (10)$$

$r = 0.949;\ s = 0.005;\ F = 45.087;\ n = 7$

Thus, the chemical shift data in Table-1 shows that the electron releasing substituent causes an upfield shift whereas the electron withdrawing substituent causes a downfield shift. The DSP analysis of C_4 carbon with various σ_R scale is given in Table-4 and the highest fit is given in eqns. 11 and 12.

$$\log \delta C_4 = 0.043 (\pm 0.010)\ \sigma_I + 0.080 (\pm 0.014)\ \sigma_R^- + 2.164 (\pm 0.002) \quad (11)$$

$R = 0.990;\ SE = 0.003;\ F = 77.778;\ n = 6$

$$\log \delta C_4 = 0.022 (\pm 0.011)\ F + 0.056 (\pm 0.010)\ R + 2.162 (\pm 0.003) \quad (12)$$

$R = 0.960;\ SE = 0.005;\ F = 23.336;\ n = 7$

The value of ρ_I and ρ_R are positive, which discloses that the normal substituent effect activates on C_4 carbon atom, *i.e.* an electron withdrawing substituent decreases the C_4 carbon atom shielding and an electron releasing substituent increases it. The magnitude of ρ_R greater than ρ_I indicates the predominance of resonance effect over inductive effect in the chemical shift of C_4 carbon atom. The results of the Yukawa-Tsuno correlation (eqn. 3) is given in Table-5 and the highest fit is given in eqn. 13:

$$\log \delta C_4 = 0.030 (\pm 0.014)\ \sigma_p^o + 0.040 (\pm 0.014)\ (\sigma_p^+ - \sigma_p^o) + 2.164 (\pm 0.005) \quad (13)$$

$R = 0.954;\ SE = 0.010;\ F = 10.197;\ n = 5$

C_6 – carbon atom: The chemical shift of C_6 carbon atom appeared over a range of 1.12 ppm. The SSP analysis results is shown in Table-3 and the correlation afforded by σ_p^- constant is given in eqn. 14:

$$\log \delta C_6 = -0.003 (\pm 0.000)\ \sigma_p^- + 2.115 (\pm 0.000) \quad (14)$$

$r = 0.963;\ s = 0.000;\ F = 63.18;\ n = 7$

The chemical shift data in Table-1 shows that the electron releasing substituent causes a downfield shift whereas the electron withdrawing substituent causes an upfield shift. The DSP analysis of C_6 carbon with various σ_R scale is also given in Table-4 and the greatest fit is given in eqns. 15 and 16:

$$\log \delta C_6 = -0.003 (\pm 0.001)\ \sigma_I - 0.006 (\pm 0.001)\ \sigma_R^o + 2.115 (\pm 0.000) \quad (15)$$

$R = 0.959;\ SE = 0.001;\ F = 23.181;\ n = 7$

$$\log \delta C_6 = -0.004 (\pm 0.002);\ F - 0.005 (\pm 0.001)\ R + 2.115 (\pm 0.001) \quad (16)$$

$R = 0.899;\ SE = 0.001;\ F = 8.461;\ n = 7$

The value of the slopes ρ_I and ρ_R are negative, which discloses that the reverse substituent effect activates on C_6 carbon atom. The Yukawa-Tsuno correlation (eqn. 3) is given in Table-5 and the greatest fit is given in eqn. 17.

$$\log \delta C_6 = -0.005 (\pm 0.002)\ \sigma_p + 0.000 (\pm 0.003)\ (\sigma_p^+ - \sigma_p) + 2.075 (\pm 0.001) \quad (17)$$

$R = 0.890;\ SE = 0.001;\ F = 7.613;\ n = 7$

C_8–carbon atom: The chemical shift of C_8 carbon atom appeared over a narrow range of 0.36 ppm. The SSP analysis results is shown in Table-3 and the correlation afforded by σ_P^o constant is given in eqn. 18:

$$\log \delta C_8 = 0.002 (\pm 0.000)\ \sigma_p^o + 2.170 (\pm 0.000) \quad (18)$$

$$r = 0.997;\ s = 0.000;\ F = 467.801;\ n = 5$$

The chemical shift data in Table-1 shows that the electron releasing substituent causes an upfield shift whereas the electron withdrawing substituent causes a downfield shift. The DSP analysis of C_8 carbon with various σ_R scale is given in Table-4 and the greatest fit is given in eqns. 19 and 20.

$$\log \delta C_8 = 0.002\ (\pm\ 0.000)\ \sigma_I + 0.001\ (\pm\ 0.000)\ \sigma_R^o + 2.170\ (\pm\ 0.000) \qquad (19)$$

$$R = 0.993;\ SE = 0.000;\ F = 148.01;\ n = 7$$

$$\log \delta C_8 = 0.002\ (\pm\ 0.000)\ F + 0.001\ (\pm\ 0.000)\ R + 2.170\ (\pm\ 0.000) \qquad (20)$$

$$R = 0.999;\ SE = 0.000;\ F = 712.431;\ n = 7$$

The value of ρ_I and ρ_R are positive, which discloses that the normal substituent effect activates on C_8 carbon atom, *i.e.* an electron-withdrawing substituent decreases the C_8 carbon atom shielding and an electron-releasing substituent increases it, which is further confirmed by using the Yukawa-Tsuno correlation (Table-5). The highest fit is given in eqn. 21.

$$\log \delta C_8 = 0.002\ (\pm\ 0.000)\ \sigma_p - 0.001\ (\pm\ 0.000)\ (\sigma_p^+ - \sigma_p) + 2.170\ (\pm\ 0.000) \qquad (21)$$

$$R = 0.998;\ SE = 0.000;\ F = 424.939;\ n = 7$$

C_{15}–carbon atom: The chemical shift of C_{15} carbon was appeared over a relatively narrow range of 0.124 ppm. The SSP analysis results shown in Table-3 confirmed the outcomes and a fairly good correlation afforded by σ_p^- constant is given in eqn. 22.

$$\log \delta C_{15} = -0.000\ (\pm\ 0.000)\ \sigma_P^- + 2.196\ (\pm\ 0.000) \qquad (22)$$

$$r = 0.964;\ s = 0.000;\ F = 39.845;\ n = 5$$

Table-1 shows that the electron-releasing substituent causes an upfield shift whereas the electron withdrawing substituent causes a downfield shift. The DSP analysis results of C_{15} carbon with various σ_R scale is given in Table-4 and the highest fit is given in eqns. 23 and 24.

$$\log \delta C_{15} = 0.000\ (\pm\ 0.000)\ \sigma_I + 0.000\ (\pm\ 0.000)\ \sigma_R^- + 2.196\ (\pm\ 0.000) \qquad (23)$$

$$R = 0.999;\ SE = 0.000;\ F = 248.264;\ n = 4$$

$$\log \delta C_{15} = -\ 0.000\ (\pm\ 0.000)\ F - 0.000\ (\pm\ 0.000)\ R + 2.196\ (\pm\ 0.000) \qquad (24)$$

$$R = 0.825;\ SE = 0.000;\ F = 3.187;\ n = 6$$

Based on eqns. 23 and 24, the results of the Yukawa-Tsuno eqn. 3, is given in Table-5. The greatest fit is given in eqn. 25.

$$\log \delta\ C_{15} = 0.000\ (\pm\ 0.000)\ \sigma_p^o - 0.000\ (\pm\ 0.000)\ (\sigma_p^+ - \sigma_p^o) + 2.196\ (\pm\ 0.000) \qquad (25)$$

$$R = 0.992;\ SE = 0.000;\ F = 62.264;\ n = 5$$

C_5–carbon atom: The chemical shift of C_5 carbon atoms appeared over a narrow range of about 0.948 ppm. The SSP analysis of C_5 σ_p, σ_p^o, σ_p^+, σ_p^-, σ_p^+/σ_p, σ_p/σ_p^- and σ_p^+/σ_p^- gave poor correlation coefficients (r) 0.711, 0.438, 0.825, 0.760, 0.770, 0.767 and 0.822, respectively. Equations 26-28 described the results of the SSP analysis that was performed.

$$\log \delta C_5 = 0.009\ (\pm\ 0.004)\ \sigma_p + 1.630\ (\pm\ 0.001) \qquad (26)$$

$$r = 0.711;\ s = 0.003;\ n = 7$$

$$\log \delta C_5 = 0.007\ (\pm\ 0.002)\ \sigma_P^+ + 1.632\ (\pm\ 0.001) \qquad (27)$$

$$r = 0.825;\ s = 0.002;\ n = 7$$

$$\log \delta C_5 = 0.006\ (\pm\ 0.002)\ \sigma_P^- + 1.630\ (\pm\ 0.001) \qquad (28)$$

$$r = 0.760;\ s = 0.003;\ n = 7$$

The DSP results of C_5 carbon with various σ_R scale is given in Table-4 and the excellent correlation is shown in eqns. 29 and 30.

$$\log \delta C_5 = 0.003\ (\pm\ 0.002)\ \sigma_I + 0.020\ (\pm\ 0.002)\ \sigma_R + 1.633\ (\pm\ 0.000) \qquad (29)$$

$$R = 0.985;\ SE = 0.001;\ F = 47.353;\ n = 6$$

$$\log \delta C_5 = -0.001\ (\pm\ 0.003)\ F + 0.015\ (\pm\ 0.003)\ R + 1.633\ (\pm\ 0.001) \qquad (30)$$

$$R = 0.948;\ SE = 0.001;\ F = 17.576;\ n = 7$$

The triple substituent parameter (TSP) analysis of Charton's steric parameter (ν) gave good correlations valus as shown in Table-6. The high correlation coefficient (R) and minimum standard error (SE) of the regression equation provide TSP analysis the best fit, as shown in eqns. 31 and 32.

$$\log \delta C_5 = -0.001\ (\pm\ 0.001)\ \sigma_I + 0.015\ (\pm\ 0.001)\ \sigma_R^o - 0.004\ (\pm\ 0.001)\ \nu + 1.634(\pm\ 0.000) \qquad (31)$$

$$R = 0.999;\ SE = 0.000;\ n = 5$$

$$\log\delta C_5 = -0.004\ (\pm\ 0.000)\ F + 0.009\ (\pm\ 0.000)\ R - 0.004\ (\pm\ 0.000)\ \nu + 1.634\ (\pm\ 0.000) \qquad (32)$$

$$R = 0.999,\ s = 0.00,\ n = 5$$

A better description of the composition of the electrical effect [26,27] is given by eqn. 33:

$$P_R = \frac{\beta 100}{\alpha + \beta + \varphi} \qquad (33)$$

where P_R is defined as the percentage of delocalized effect. The result of the TSP analysis (Table-6) shows that the delocalized effect is predominant over the localized effect and the magnitude (%) of the steric factor [26] is represented by eqn. 34 which confirmed that the steric effect is also operating to some extent.

TABLE-6
TSP ANALYSIS OF SCS DATA OF C_5 CARBON ATOMS OF $1^4,1^5,3^4,3^5,9^4,9^5,11^4,11^5$-OCTAMETHOXY-2,10-*BIS*(4-METHOXYPHENYL)-4,8,12,16-TETRAAZA-1,3,9,11(1,2),6,14(1,4)-HEXABENZENA CYCLOHEXADECAPHANE-4,7,12,15-TETRAENE COMPOUNDS EMPLOYING eqn. 33

Scale	α	β	φ	R	s	F	P_R	P_S
σ_I, σ_R, ν	-0.002 ± 0.001	0.009 ± 0.001	-0.005 ± 0.001	0.998	0.000	69.191	56.2	31.2
σ_I, σ_R^o, ν	-0.001 ± 0.001	0.015 ± 0.001	-0.004 ± 0.001	0.999	0.000	178.454	75.0	20.0
σ_I, σ_R^+, ν	-0.008 ± 0.005	0.003 ± 0.002	-0.003 ± 0.006	0.918	0.002	1.781	21.4	21.4
σ_I, σ_R-, ν	0.002 ± 0.004	0.017 ± 0.006	-0.002 ± 0.003	0.981	0.001	8.303	80.9	9.5
F, R, ν	-0.004 ± 0.000	0.009 ± 0.000	-0.004 ± 0.000	0.999	0.000	20129.8	52.9	23.5

$$\mathrm{Ps} = \frac{\varphi 100}{\alpha + \beta + \varphi} \quad (34)$$

Conclusion

A series of substituted macrocyclic compounds were synthesized by the condensation of substituted benzaldehydes with 1,2-dimethoxy benzene followed by nitration, reduction and cyclization with terephthaldehyde. The synthesized substituted molecules were characterized by the ^{1}H & ^{13}C spectral data. The ^{13}C NMR spectral data of the substituted macrocyclic compounds have been correlated with Hammett substituent constants and F and R parameters. The ^{13}C NMR spectral correlations produced the greatest number of satisfactory correlations.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. E. Rosta and A. Warshel, *J. Chem. Theory Comput.*, **8**, 3574 (2012); https://doi.org/10.1021/ct2009329
2. J. Shorter, Correlation Analysis in Organic Chemistry, An Introduction to Linear Free Energy Relationship, London, p. 119 (1973).
3. D. Iguchi, D. Ravelli, R. Erra-Balsells and S.M. Bonesi, *Molecules*, **25**, 2061 (2020); https://doi.org/10.3390/molecules25092061
4. C. Hansch, A. Leo and R.W. Taft, *Chem. Rev.*, **91**, 165 (1991); https://doi.org/10.1021/cr00002a004
5. A. Ikezaki, T. Ikeue and M. Nakamura, *Inorg. Chim. Acta*, **335**, 91 (2002); https://doi.org/10.1016/S0020-1693(02)00819-8
6. N.Y. Gorobets, S.A. Yermolayev, T. Gurley, A.A. Gurinov, P.M. Tolstoy, I.G. Shenderovich and N.E. Leadbeater, *J. Phys. Org. Chem.*, **25**, 287 (2012); https://doi.org/10.1002/poc.1910
7. C. Bustos, L. Alvarez-Thon, E. Molins, I. Moreno-Villoslada, G. Vallejos-Contreras, C. Sánchez, X. Zarate, D. Mac-Leod Carey and E. Schott, *J. Mol. Struct.*, **1171**, 349 (2018); https://doi.org/10.1016/j.molstruc.2018.05.088
8. H. Yuan, P.-W. Chen, M.-Y. Li, Y. Zhang, Z.-W. Peng, W. Liu, R.S. Paton and C. Cao, *J. Mol. Struct.*, **1204**, 127489 (2020); https://doi.org/10.1016/j.molstruc.2019.127489
9. M.B. Smith and J. March, March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, Wiley: Hoboken, NJ, USA, edn, 6, p. 401 (2007).
10. F.A. Carey and R.J. Sundberg, Advanced Organic Chemistry, Part A: Structure and Mechanisms, Springer: Berlin/Heidelberg, Germany, edn. 5, p. 335 (2007).
11. F.A. Carroll, Perspectives on Structure and Mechanism in Organic Chemistry; John Wiley & Sons: Hoboken, NJ, USA, p. 366 (1998).
12. J.H. Markgraf, L. Hong, D.P. Richardson and M.H. Schofield, *Magn. Reson. Chem.*, **45**, 985 (2007); https://doi.org/10.1002/mrc.2082
13. H.S. Lee, J.S. Yu and C.K. Lee, *Bull. Korean Chem. Soc.*, **30**, 2351 (2009); https://doi.org/10.5012/bkcs.2009.30.10.2351
14. N. Kalyanasundaram, S.P. Sakthinathan, R. Suresh, D. Kamalakkannan, S. John Joseph, G. Vanangamudi and G. Thirunarayanan, *Int. Lett. Chem. Phys. Astron*, **28**, 23 (2014); https://doi.org/10.56431/p-4z1nao
15. D.J. Craik and R.T.C. Brownlee, *Prog. Phys. Org. Chem.*, **14**, 1 (1983); https://doi.org/10.1002/9780470171936.ch1
16. N.B. Chapman and J. Shorter, Advances in Linear Free Energy Relationships, Plenum: London (1972).
17. L.P. Hammett, Physical Organic Chemistry, McGraw Hill Book Company, Inc., New York, Chapter VII, (1970).
18. K. Radhakrishnan, P. Senthilkumar, P.K. Manikandan and U.K. Ray, *J. Adv. Sci. Res.*, **12**, 198 (2021).
19. P. Senthilkumar, K. Radhakrishnan and P.K. Manikandan, *World J. Pharm. Res.*, **11**, PP1103 (2022).
20. R. Arulkumaran, V. Manikandan and G. Thirunarayanan, *World Sci. News*, **80**, 235 (2017).
21. R. Arulkumaran, V. Manikandan, P. Christhuraj and G. Thirunarayanan, *World Sci. News*, **62**, 93 (2017).
22. G. Thirunarayanan, K.G. Sekar and R.L. Narayanan, *Int. Lett. Chem., Phys. Astron.*, **32**, 88 (2014); https://doi.org/10.56431/p-4kg378
23. M. Rajarajan, R. Senbagam, V. Vijayakumar, V. Manikandan, S. Balaji, G. Vanangamudi and G. Thirukumaran, *World Sci. News*, **9**, 155 (2015).
24. G. Thirunarayanan, M. Gopalakrishnan and G. Vanangamudi, *Spectrochim. Acta A Mol. Biomol. Spectrosc.*, **67**, 1106 (2007); https://doi.org/10.1016/j.saa.2006.09.034
25. G. Thirunarayanan, *Bull. Chem. Soc. Ethiop.*, **28**, 73 (2014); https://doi.org/10.4314/bcse.v28i1.9
26. J.E. Arrowsmith, M.J. Cook and D.J. Hardstone, *Org. Magn. Reson.*, **11**, 160 (1978); https://doi.org/10.1002/mrc.1270110314
27. P. Mohandass, K. Radhakrishnan, S. Manimekalai, V. Suriyanarayanan and S. Radhakrishnan, *Asian J. Res. Chem*, **11**, 43 (2018); https://doi.org/10.5958/0974-4150.2018.00010.X